Titanium(III)-Induced Transformation of Hydroxylamines to Imines or Secondary Amines

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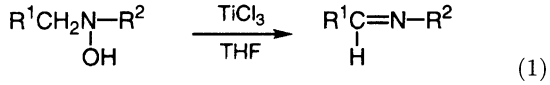
N,N-Disubstituted and cyclic hydroxylamines can be converted into the corresponding imines efficiently upon treatment with anhydrous titanium trichloride in THF at room temperature. Similar treatment of *N*-allylhydroxylamines with anhydrous titanium trichloride gives 1-azadienes, which are versatile synthetic intermediates for aza-Diels–Alder reactions. On the other hand, the same hydroxylamines can be converted into the corresponding secondary amines upon treatment with aqueous titanium trichloride in methanol. It is noteworthy that optically active hydroxylamines, which have chirality at the α-position to nitrogen, can be converted into optically active secondary amines without loss of chirality. Dihydro-2(1*H*)-quinolinones can be prepared upon treatment of 1-hydroxy-3,4-dihydro-2(1*H*)-quinolinones with aqueous titanium trichloride. The substrates of *N,N*-disubstituted and cyclic hydroxylamines can be prepared readily upon treatment of nitrones with nucleophiles. Since nitrones can be prepared by metal-catalyzed oxidations of secondary amines with hydrogen peroxide, the present titanium(III)-promoted reaction of hydroxylamines will provide a convenient method for the synthesis of either α-substituted imines or amines from secondary amines.

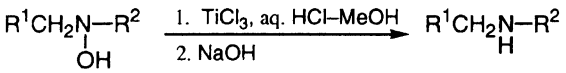
Imines are important synthetic intermediates for the synthesis of alkaloids,[1] amino acids,[2] amino sugars,[3] and β-lactams.[4] Generally, imines are prepared by condensation of carbonyl compounds with amines.[5] Cyclic imines, which are key intermediates for the synthesis of nitrogen-containing naturally occurring compounds, have been prepared by Bischlar–Napieralsky reaction,[6] elimination reactions of *N*-chloroamines or nitrosoamines,[7] catalytic oxidation of secondary amines with *t*-BuOOH,[8] and other methods.[9] The reported dehydrations of hydroxylamines are limited to few reactions, which include thermal decomposition and base-induced reaction of hydroxylamines.[10]

We have found that dehydration of *N,N*-disubstituted and cyclic hydroxylamines proceeds highly efficiently upon treatment with anhydrous $TiCl_3$ in THF under mild reaction conditions to give linear and cyclic imines



(1)

as depicted in Eq. 1. In contrast, the reduction of *N,N*-disubstituted hydroxylamines is performed upon treatment with aqueous $TiCl_3$ in HCl solution followed by aqueous NaOH to give secondary amines as depicted by Eq. 2.[11]



(2)

Although aqueous $TiCl_3$-mediated reductive cleavage of N–O bonds of hydroxylamines was reported, the substrates were limited to *N*-hydroxyimidazoles[12a] and *N*-hydroxyazetizinones.[12b] The present reaction provides a general and convenient method for reductive transformation of *N,N*-disubstituted hydroxylamines to secondary amines.

The substrates of *N,N*-disubstituted and cyclic hydroxylamines can be prepared readily from the nitrones derived from the catalytic oxidation of secondary amines with hydrogen peroxide,[13—15] upon treatment with various nucleophiles.[13a,16,17] Therefore, the present titanium(III)-promoted reaction of hydroxylamines will provide a convenient method for the synthesis of either α-substituted imines or amines from secondary amines (Chart 1).

Results and Discussion

Synthesis of Imines. *N,N*-Disubstituted and cyclic hydroxylamines can be converted into the corresponding imines upon treatment with anhydrous $TiCl_3$ in THF at room temperature for 15 min. The activity of various metal salts has been examined for the reactions of *N,N*-dibenzylhydroxylamine (**1**) and 2-hydroxy-1,2,3,4-tetrahydroisoquinoline (**3**). The treatment with an equivalent of $TiCl_3$ in dry THF gave an excellent result. Lewis acids such as $AlCl_3$ and $TiCl_4$ gave no dehydrated product. The solvent effect for the dehydration is drastic. The dehydration proceeds efficiently only in dry THF. Using other solvents such as benzene, ether, and CH_2Cl_2, dehydrated product was not obtained.

The representative results of the reaction of *N,N*-disubstituted and cyclic hydroxylamines with anhydrous $TiCl_3$ are summarized in Table 1. Generally, the dehydration proceeds quite smoothly and regiose-

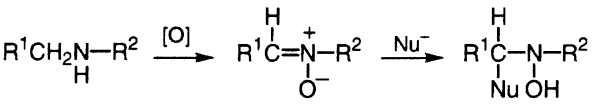


Chart 1.

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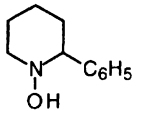
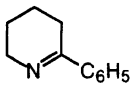
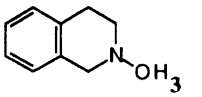
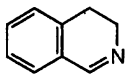
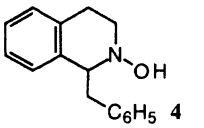
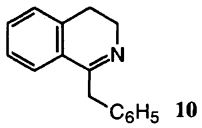
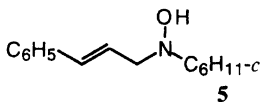
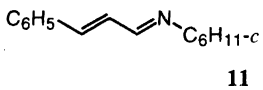
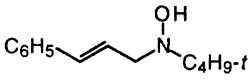
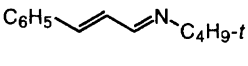
Table 1. Dehydration of Hydroxylamines with Anhydrous $TiCl_3$[a)]

Entry	Hydroxylamine	Imine	Isolated yield/%
1	$C_6H_5CH_2N(OH)CH_2C_6H_5$ **1**	$C_6H_5CH{=}NCH_2C_6H_5$ **7**	78
2	 **2**	 **8**	70
3	 **3**	 **9**	89
4	 **4**	 **10**	66
5	 **5**	 **11**	53
6	 **6**	 **12**	60

a) Hydroxylamines were treated with an equivalent of anhydrous $TiCl_3$ in THF at room temperature for 15 min—1 h.

lectively at room temperature, and the regioisomers can not be detected among the products. Since anhydrous $TiCl_3$ is not soluble in THF, a solution of a hydroxylamine is added dropwise to a suspension of $TiCl_3$ in THF with vigorous stirring under argon. Since hydroxylamines can be prepared upon treatment of nitrones derived from catalytic oxidation of secondary amines[13—15] with Grignard reagents, the combination of these reactions will provide a versatile and convenient method for the synthesis of substituted imines from secondary amines. Typically, 1-benzyl-2-hydroxy-1,2,3,4-tetrahydroisoquinoline (**4**), which is derived from the oxidation of 1,2,3,4-tetrahydroisoquinoline followed by treatment with benzylmagnesium bromide, underwent the dehydration to give imine **10** in 66% yield

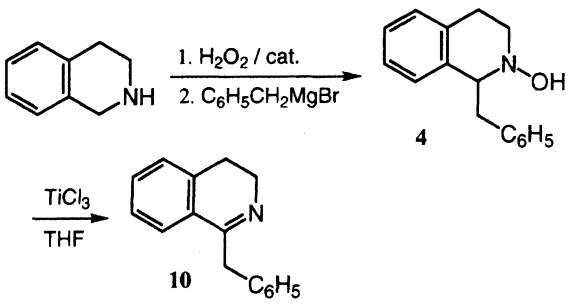


Chart 2.

(Chart 2). It is noteworthy that the reaction of 2-cyano-1-hydroxypiperidine with anhydrous $TiCl_3$ afforded 2-piperidinone in 71% yield in place of 2-cyano-3,4,5,6-tetrahydropyridine.

Allylic hydroxylamines can be converted into the corresponding azadienes, which are versatile synthetic intermediates for aza-Diels–Alder reactions.[18] Thus, *N*-allylhydroxylamines **5** and **6** can be converted into the corresponding 1-aza-1,3-dienes **11** and **12** in 53 and 60% yields, respectively (Entries 5 and 6). Since the substrates of allylic hydroxylamines have been prepared readily by the palladium(0)-catalyzed reaction of allylic acetates with hydroxylamines,[19] azadienes can be prepared readily from allyl acetates (Chart 3).

Synthesis of Secondary Amines. In contrast to the reaction of hydroxylamines with anhydrous $TiCl_3$, the reaction of hydroxylamines with two equivalents of aqueous $TiCl_3$ in HCl solution gives the corresponding secondary amines. Although the reductive cleavage of the N–O bonds of hydroxylamines has been performed

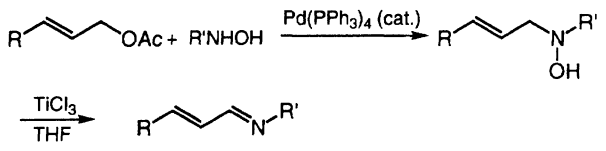
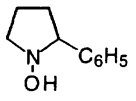
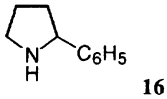
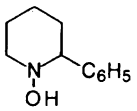
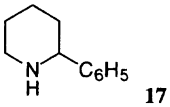
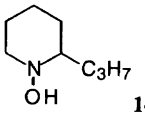
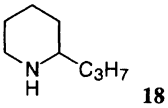
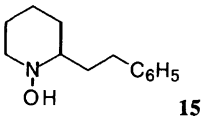
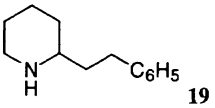
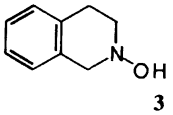
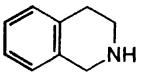


Chart 3.

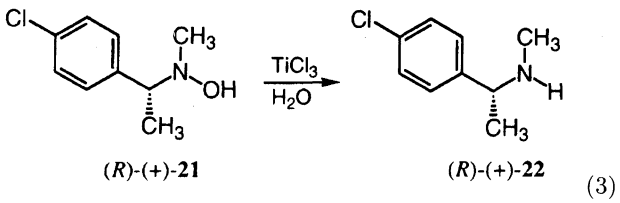
Table 2. Reduction of Hydroxylamines with Aqueous $TiCl_3$[a)]

Entry	Hydroxylamine	Amine	Isolated yield/%
1	 **13**	 **16**	69
2	 **2**	 **17**	91
3	 **14**	 **18**	86
4	 **15**	 **19**	96
5	 **3**	 **20**	79

a) Hydroxylamines were treated with two equivalents of aqueous $TiCl_3$ in methanol at room temperature for 15 min—1 h.

by the reduction with Zn/HCl[19,20] and catalytic hydrogenation,[21] the present reaction is convenient because of simple operation, mild reaction conditions, and toleration of the carbon–carbon double bonds. The representative results of the reduction of hydroxylamines are summarized in Table 2. It is noteworthy that the secondary amines thus obtained are not derived from the reduction of imines, because the treatment of imines **7** and **9** with aqueous $TiCl_3$ did not give the corresponding secondary amines under the reaction conditions.

Moreover, optically active secondary amines can be obtained by the reduction of optically active hydroxylamines, which are prepared by ruthenium-catalyzed asymmetric hydrosilylation of nitrones.[22] Typically, the treatment of (*R*)-(+)-*N*-[1-(4-chlorophenyl)ethyl]-*N*-methylhydroxylamine (**21**) (98% ee) with aqueous $TiCl_3$ gave (*R*)-(+)-*N*-methyl-1-(4-chlorophenyl)ethylamine (**22**) (98% ee) (Eq. 3).



(*R*)-(+)-**21** (*R*)-(+)-**22** (3)

The present $TiCl_3$- mediated reduction of hydroxylamines can be applied to the reduction of cyclic hydroxamic acids to lactams. Thus, the treatment of 1-hydroxy-3,4-dihydro-2(1*H*)-quinolinones with aqueous $TiCl_3$ under the same reaction conditions gives the corresponding 3,4-dihydro-2(1*H*)-quinolinones, which have potent physiological activities such as β-adrenergic blocking action.[23] The representative results are summarized in Table 3. Since the substrates of 1-hydroxy-3,4-dihydro-2(1*H*)-quinolinones have been prepared simply by catalytic hydrogenation of quinolines under water-gas-shift conditions[24] followed by the tungstate-catalyzed hydrogen peroxide oxidation,[25] the present reaction provides a convenient method for synthesis of dihydro-2(1*H*)-quinolinones from quinolines (Chart 4).

Mechanism. Aqueous $TiCl_3$ has been used for dismutation of secondary nitroalkanes[26a] and reduction of aromatic nitro compounds,[26b] nitrosoamines,[26c] *N*-hydroxyimidazoles,[12a] and *N*-hydroxyazetidinones.[12b] The reduction of *N*,*N*-disubstituted hydroxylamines with aqueous $TiCl_3$ in aqueous HCl solution can be rationalized by assuming the double one-electron transfer mechanism (Chart 5). Electron transfer from $TiCl_3$ to

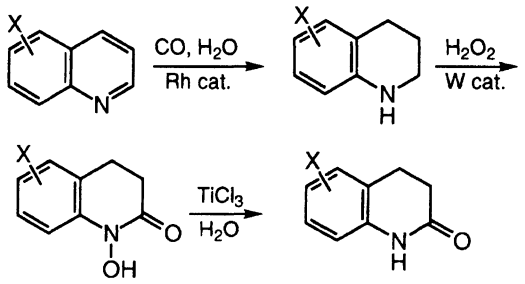
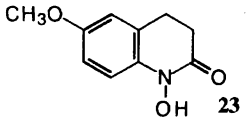
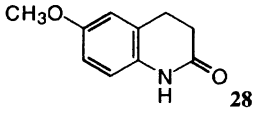
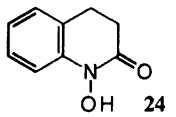
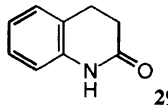
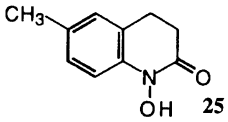
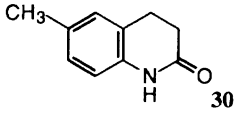
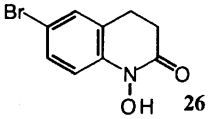
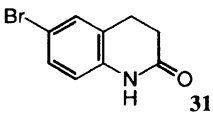
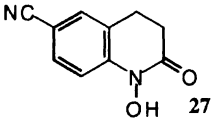
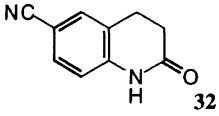


Chart 4.

Table 3. Reduction of Hydroxamic Acids with Aqueous $TiCl_3$[a)]

Entry	Hydroxamic Acid	Lactam	Isolated yield/%
1	 **23**	 **28**	98
2	 **24**	 **29**	84
3	 **25**	 **30**	99
4	 **26**	 **31**	86
5	 **27**	 **32**	99

a) Hydroxylamines were treated with two equivalents of aqueous $TiCl_3$ in THF at room temperature for 1 h.

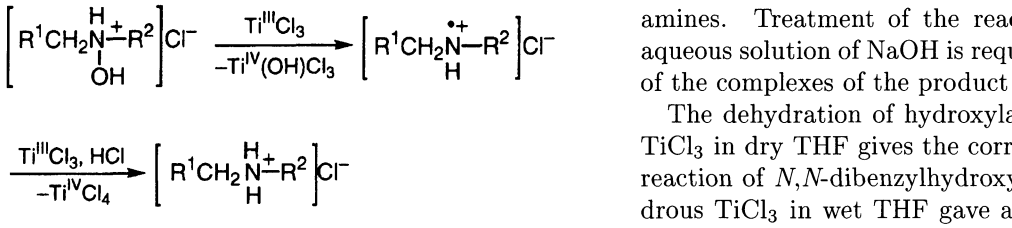


Chart 5.

coordinated *N,N*-disubstituted hydroxylamine followed by extrusion of hydroxyl group would give aminiumyl radical.[27)] Intermediacy of aminiumyl radical has been postulated in the vinyl polymerization induced by $TiCl_3$ and NH_2OH.[28)] Further electron transfer to the aminiumyl radical from $TiCl_3$ followed by protonation would give the corresponding secondary amine hydrochloride. As shown in Table 4, two equivalents of $TiCl_3$ are required for the reduction of *N,N*-disubstituted hydroxylamines. Treatment of the reaction mixture with an aqueous solution of NaOH is required for decomposition of the complexes of the product with Ti(IV) species.

The dehydration of hydroxylamines with anhydrous $TiCl_3$ in dry THF gives the corresponding imines. The reaction of *N,N*-dibenzylhydroxylamine (**1**) with anhydrous $TiCl_3$ in wet THF gave a mixture of *N*-benzylidenebenzylamine (**7**) and dibenzylamine, indicating the presence of a common intermediate. The stoichiometry of $TiCl_3$ for the dehydration of **1** is shown in Table 5. Although an equivalent of $TiCl_3$ was used, consumed $TiCl_3$ was only 4 mol%, indicating that Ti(III) species can be used catalytically. Electron transfer to the coordinated hydroxylamines **33** from Ti(III) followed by extrusion of hydroxide would give aminyl radical **34** (Chart 6). 1,2-Hydrogen shift from the α carbon to the nitrogen would form α-aminoalkyl radical **35**,[30)] which

Table 4. Stoichiometry of $TiCl_3$ for the Reduction of **1**[a)]

Run	$TiCl_3$ mmol	Hydroxylamine mmol	$TiCl_3$ consumed[b)] mmol	Stoichiometry
1	11.11	0.789	1.56	1.98
2	11.03	0.892	1.76	1.97
3	11.23	0.892	1.89	2.12

a) The procedure is described in the experimental section. b) The excess of $TiCl_3$ was titrated with an Fe(III) solution.[29)]

Table 5. Stoichiometry of $TiCl_3$ for the Dehydration of **1**[a)]

Run	$TiCl_3$ mmol	Hydroxylamine mmol	$TiCl_3$ consumed[b)] mmol	Stoichiometry
1	2.15	1.40	0.05	0.04
2	2.05	1.27	0.05	0.04
3	2.13	1.30	0.10	0.08

a) The procedure is described in the experimental section. b) The excess amount of $TiCl_3$ in the dehydration of **1** was titrated with an Fe(III) solution.[29)]

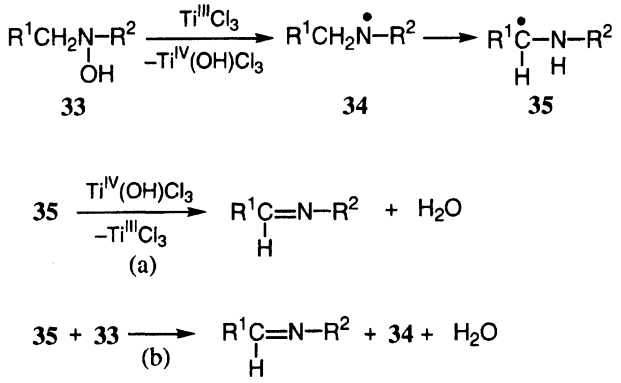


Chart 6.

undergoes electron transfer to $Ti^{IV}(OH)Cl_3$ species to give imine (path a). It is known that aminoalkyl radicals are readily converted into imines by electrochemical process.[31] Alternatively, the reaction of α-aminoalkyl radical **35** with hydroxylamine **33** would give aminyl radical **34** again along with imine and water to complete radical chain process (path b). In any way, the radical intermediate thus formed seem to be complexed with titanium rather than free, as proposed in the metal ion-catalyzed reactions of *N*-chloroamines.[32]

Experimental

General. ^1H and/or ^{13}C NMR spectra were recorded on JEOL JNM-PMX 60 SI, JEOL FA-90A, JEOL JNM-FX-100, JEOL JNM-GSX-270, and Bruker AC-300 spectrometers in $CDCl_3$. IR spectra were recorded on Hitachi 215 and Shimadzu IR-400 spectrometers. Mass spectra were obtained on a Hitachi RMS-4 or Shimadzu GCMS-QP1000 mass spectrometer. Elemental analyses were performed on a Yanagimoto MT-3 CHN corder. Melting points were determined by Yanagimoto micro melting point apparatus.

Materials. Anhydrous (assay, 81—100%) and aqueous $TiCl_3$ (assay, 1.61 M; 1 M=1 mol dm^{-3}) were commercially available from Wako Pure Chemical Industries and used without purification. Methanol and tetrahydrofuran (THF) were distilled before use. All reactions of *N,N*-disubstituted and cyclic hydroxylamines with $TiCl_3$ were carried out under argon. *N,N*-Disubstituted and cyclic hydroxylamines,[13b,22] *N*-allylhydroxylamines,[19] and hydroxamic acids[24] were prepared according to the reported procedures, and the spectral data of new compounds are listed below.

Assay of Anhydrous $TiCl_3$ and Aqueous $TiCl_3$.[29] Ti(III) content in commercial anhydrous $TiCl_3$ was assayed as follows. An exactly weighed powder of $TiCl_3$ was dissolved in 1 M H_2SO_4 (10 mL) with stirring for 30 min at room temperature. The resulting solution was titrated with a standard $Fe(NH_4)(SO_4)_2$ solution under argon, using a 10% KSCN as an indicator. An aqueous $TiCl_3$ in 1 M H_2SO_4 was also titrated with a standard $Fe(NH_4)(SO_4)_2$ solution under argon.

1-Hydroxy-2-phenylpiperidine (2): Mp 109.5—111.5 °C; IR (Nujol) 1950, 1890, 1820, 1750, 1075, 1100, 1065, 1040, 950, 900, 872, 742, 690 cm^{-1}; ^1H NMR (270 MHz) δ=1.25—1.43 (m, 1H, H-4$_{ax}$), 1.52—1.85 (m, 5H), 2.58 (ddd, J=14.0, 9.4, 2.9 Hz, 1H, H-6$_{ax}$), 3.27 (d, J=9.4 Hz, 1H, H-6$_{eq}$), 3.35 (dd, J=11.2, 2.8 Hz, 1H, H-2), 4.84 (br, 1H, OH), 7.20—7.38 (m, 5H, ArH); ^{13}C NMR (76 MHz) δ=24.1 (C-4), 25.9 (C-5), 35.4 (C-3), 58.7 (C-6), 73.6 (C-2), 127.2 (*o*), 127.3 (*p*), 128.5 (*m*), 143.5 (*i*). Found: C, 74.41; H, 8.55; N, 7.87%. Calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90%.

1-Benzyl-2-hydroxy-1,2,3,4-tetrahydroisoquinoline (4): Mp 99—101 °C; IR (KBr) 2950, 1740, 1605, 1498, 1454, 1370, 1245, 1210, 1082, 1030, 950, 912, 750, 695 cm^{-1}; ^1H NMR (300 MHz) δ=2.88 (dd, J=10.2, 5.1 Hz, 2H, H-4), 3.00 (dd, J=11.9, 6.1 Hz, 1H, H-3), 3.10 (dd, J=13.8, 8.5 Hz, 1H, CH_2Ph), 3.24 (dd, J=14.0, 6.1 Hz, 1H, CH_2Ph), 3.25 (dd, J=14.0, 5.2 Hz, 1H, H-3), 4.37 (dd, J=8.5, 5.2 Hz, 1H, H-1), 7.10—7.36 (m, 9H, ArH); ^{13}C NMR (76 MHz) δ=25.7 (C-4), 41.2, 50.0 (C-3), 66.1 (C-1), 125.7, 126.1, 126.3, 127.4, 128.3, 128.4, 129.4, 133.3, 136.6, 139.5. Found: C, 80.27; H, 7.20; N, 5.89%. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85%.

***N*-Cinnamyl-*N*-cyclohexylhydroxylamine (5):** ^1H NMR (60 MHz) δ=1.10—2.33 (m, 10H), 2.67—3.29 (m, 1H), 3.73 (d, J=6.0 Hz, 2H, H-1), 6.17 (dt, J=15.0 and 6.0 Hz, 1H, H-2), 6.47 (d, J=15.0 Hz, 1H, H-3), 7.10—7.43 (m, 6H, ArH, OH).

***N*-Cinnamyl-*N*-*t*-butylhydroxylamine (6):** ^1H NMR (60 MHz) δ=1.15 (s, 9H, *t*-C_4H_9), 3.42 (d, J=5.5 Hz, 2H, H-1), 6.30 (dt, J=15.0, 5.5 Hz, 1H, H-2), 6.50 (d, J=15.0 Hz, 1H, H-3).

1-Hydroxy-2-phenylpyrrolidine (13): Bp 150—160 °C/3.5 mmHg (Kugelrohr, 1 mmHg=133.3 Pa); IR (neat) 2950, 2850, 1608, 1495, 1455, 1375, 1310, 1290, 1185, 1095, 1030, 1008, 900, 748, 695 cm^{-1}; ^1H NMR (300 MHz) δ=1.72—1.88 (m, 3H), 2.14—2.18 (m, 1H, H-3), 2.74—2.84 (m, 1H, H-5), 3.13—3.20 (m, 1H, H-5), 3.73 (dd, J=9.3, 8.0 Hz, 1H, H-2), 7.15—7.40 (m, 5H, ArH); ^{13}C NMR (76 MHz) δ=19.7 (C-4), 30.1 (C-3), 57.3 (C-5), 72.5 (C-2), 127.3 (*o*), 127.7 (*m*), 128.3 (*p*), 141.4 (*i*); MS (80 eV) *m/z* (rel intensity) 164 (M^++1, 11), 163 (M^+, 84), 145 (17), 118 (100), 117 (80), 104 (45), 91 (75), 86 (58), 85 (33), 77 (37).

1-Hydroxy-2-propylpiperidine (14): IR (neat) 3175 (OH), 2925, 1640, 1445, 1372, 1360, 1345, 1268, 1236, 1148, 1100, 1002, 990, 972, 945, 875, 860, 828, 772 cm^{-1}; ^1H NMR (300 MHz) δ=0.92 (t, J=7.0 Hz, 3H), 1.08—1.49 (m, 6H), 1.49—1.77 (m, 3H), 1.84 (br-d, J=9.5 Hz, 1H, H-1′), 2.02 (br-t, J=10.8 Hz, 1H, H-1′), 2.26 (br-s, 1H, H-2), 2.51 (dt, J=10.3, 1.6 Hz, 1H, H-6), 3.27 (br-d, J=10.3 Hz, 1H, H-6); ^{13}C NMR (76 MHz) δ=14.4, 19.0, 23.7, 25.7, 30.9, 35.4, 59.6 (C-6), 67.4 (C-2).

***(R)*-(+)-*N*-[1-(4-Chlorophenyl)ethyl]-*N*-methylhydroxylamine (21):**[22] $[\alpha]_D^{25}$ +41.8° (*c* 0.476, EtOH, 97% ee); mp 95.0—97.0 °C; ^1H NMR (270 MHz) δ=1.44 (d, J=6.6 Hz, 3H, H-2), 2.49 (s, 3H, NCH_3), 3.64 (q, J=6.6 Hz, 1H, H-1), 7.22—7.31 (m, 5H); ^{13}C NMR (68 MHz) δ=19.9 (C-2), 45.8 (NCH_3), 68.5 (C-1), 128.6, 129.3, 133.2, 140.7.

Found: C, 58.38; H, 6.57; N, 7.54; Cl, 18.84%. Calcd for $C_9H_{12}NO$: C, 58.21; H, 6.51; N, 7.54; Cl, 19.12%.

Anhydrous $TiCl_3$-Induced Dehydration of Hydroxylamines to Imines. General Procedure: The preparation of *N*-benzylidenebenzylamine (**7**) is described as a typical example. To a suspension of $TiCl_3$ (assay 84%, 0.077 g, 0.42 mmol) in THF (4.2 mL) was added dropwise a solution of *N,N*-dibenzylhydroxylamine (**1**) in THF (0.5

M, 0.84 mL, 0.42 mmol) with stirring at room temperature. After the mixture was stirred for 15 min, the solvent was evaporated and 1 M NaOH was added. Extraction with CH_2Cl_2 and distillation gave **7** (0.064 g, 78%). An authentic sample was prepared by condensation of benzaldehyde with benzylamine.

Reaction of *N*,*N*-Dibenzylhydroxylamine (1) with Other Metal Salts. The reaction of **1** with $AlCl_3$ or $TiCl_4$ (one molar equivalent) was carried out according to the procedure described above. By usual work-up, starting hydroxylamine **1** was recovered in 77 and 63% yield, respectively.

Reaction of 2-Hydroxy-1,2,3,4-tetrahydroisoquinoline (3) with Other Metal Salts. The reaction of **3** with $AlCl_3$ or $TiCl_4$ (one molar equivalent) was carried out according to the procedure described above. By usual work-up, starting hydroxylamine **3** was recovered in 80 and 84% yield, respectively.

2-Phenyl-3,4,5,6-tetrahydropyridine (8): Bp 105—115 °C/2 mmHg (Kugelrohr); IR (neat) 3060, 2980, 2860, 1640, 1582, 1498, 1450, 1358, 1334, 1282, 1242, 1062, 1018, 918, 762, 692 cm^{-1}; ^1H NMR (300 MHz) δ=1.47—1.60 (m, 2H, H-5), 1.63—1.71 (m, 2H, H-4), 2.43—2.49 (m, 2H, H-3), 3.67—3.72 (m, 2H, H-6), 7.19—7.31 (m, 3H), 7.62—7.65 (m, 2H); ^{13}C NMR (76 MHz) δ=19.4 (C-4), 21.5 (C-5), 31.0 (C-3), 54.5 (C-6), 125.8 (*o*), 128.1 (*m*), 129.1 (*p*), 139.9 (*i*), 165.3 (C-2).

3,4-Dihydroisoquinoline (9): Bp 95—105 °C/3 mmHg (Kugelrohr). The IR and NMR spectra were identical with those of an authentic compound.[8b]

1-Benzyl-3,4-dihydroisoquinoline (10): IR (neat) 3070, 3030, 2940, 2900, 2850, 1612 (C=N), 1601, 1574, 1500, 1458, 1430, 1342, 1300, 1240, 1030, 866, 794, 733, 707, 693 cm^{-1}; ^1H NMR (300 MHz) δ=2.71 (t, J=7.4 Hz, 2H, H-4), 3.67 (t, J=7.4 Hz, 2H, H-3), 4.08 (s, 2H, CH_2Ph), 7.14—7.47 (m, 9H, ArH); ^{13}C NMR (76 MHz) δ=26.1 (C-4), 42.9, 47.1 (C-3), 125.7, 126.3, 126.8, 127.5, 128.5, 128.7, 130.5, 133.7, 137.9, 138.0, 166.0 (C-1); MS *m/z* 223 (M^++2, 8), 222 (M^++1, 37), 221 (M^+, 100), 115 (14), 104 (14), 91 (25), 77 (23), 65 (18), 63 (14).

Synthesis of 1-Aza-1,3-dienes. *N*-Cinnamylidenecyclohexylamine (11): To a suspension of $TiCl_3$ (0.310 g, 2.01 mmol) in THF (2 mL) was added dropwise a solution of *N*-cinnamyl-*N*-cyclohexylhydroxylamine (**5**) (0.231 g, 1.00 mmol) in THF (2 mL) at room temperature. After the mixture was stirred for 1 h, the reaction mixture was extracted with CH_2Cl_2. The extracts were dried and evaporated. To the residue was added saturated aqueous $NaHSO_4$ and the basic mixture was extracted with CH_2Cl_2. The extracts were dried (Na_2SO_4), evaporated, and Kugelrohr distillation gave **11** as a colorless oil (0.111 g, 53%): Bp 170—180 °C/0.10 mmHg (Kugelrohr); IR (neat) 3040, 2930, 2860, 1638, 1622, 1498, 1450, 1382, 1350, 1300, 1260, 1170, 1075, 982, 960, 890, 746, 685 cm^{-1}; ^1H NMR (60 MHz) δ=1.10—2.00 (m, 10H), 2.80—3.30 (m, 1H, H-1′), 6.88 (d, J=4 Hz, 2H), 7.14—7.61 (m, 5H, ArH), 8.03 (t, J=4 Hz, 1H, H-1); MS *m/z* (rel intensity) 215 (M^++2, 1), 214 (M^++1, 14), 213 (M^+, 83), 212 (77), 184 (32), 170 (42), 156 (51), 136 (21), 130 (100), 122 (35), 116 (30), 115 (100), 91 (24), 77 (20), 55 (46). An authentic sample was prepared by condensation of cyclohexylamine with cynnamaldehyde.

***N*-Cinnamylidene-*t*-butylamine (12):** Bp 185 °C/0.10 mmHg (Kugelrohr); IR (neat) 3040, 2970, 1960, 1880, 1810, 1730, 1680, 1632, 1620, 1498, 1478, 1450, 1390, 1360, 1295, 1218, 1130, 1122, 1070, 1030, 985, 905, 745, 682 cm^{-1}; ^1H NMR (60 MHz) δ=1.23 (s, 9H, C_4H_9), 6.82 (d, J=4 Hz, 2H), 7.02—7.47 (m, 5H, ArH), 7.92 (t, J=4 Hz, 1H, H-1). An authentic sample was prepared by condensation of *t*-butylamine with cinnamaldehyde.

Aqueous $TiCl_3$-Promoted Reduction of Hydroxylamines to Secondary Amines. General Procedure: The preparation of 2-phenylpiperidine (**17**) is described as a typical example. To an aqueous $TiCl_3$ (1.64 M, 1.37 mL, 2.25 mmol) was added a solution of 1-hydroxy-2-phenylpiperidine (**2**) (0.150 g, 0.85 mmol) in methanol (3 mL) and 12 M HCl (3.0 mL) at room temperature. After the mixture was stirred for 15 min, 1 M NaOH was added. The mixture was extracted with ether. The combined extracts were dried ($MgSO_4$) and evaporated to give **17** (0.124 g, 91%): IR (neat) 2960, 1642, 1598, 1585, 1490, 1462, 1438, 1352, 1258, 1218, 1060, 748, 688 cm^{-1}; ^1H NMR (300 MHz) δ=1.48—1.66 (m, 4H), 1.78 (br-d, J=10.9 Hz, 1H, H-3), 1.87 (br-d, J=10.9 Hz, 1H, H-3), 2.72 (dt, J=3.3, 12.0 Hz, 1H, H-6), 3.03 (s, 1H, NH), 3.14 (br-d, J=11.4 Hz, 1H, H-6), 3.56 (dd, J=10.5, 1.4 Hz, 1H, H-2), 7.19—7.41 (m, 5H); ^{13}C NMR (76 MHz) δ=25.2, 25.5, 34.6 (C-3), 47.6 (C-6), 62.2 (C-2), 126.7, 127.1, 128.4, 144.8 (*i*).

2-Phenylpyrrolidine (16): IR (neat) 2960, 1642, 1598, 1585, 1490, 1462, 1438, 1352, 1258, 1218, 1060, 748, 688 cm^{-1}; ^1H NMR (60 MHz) δ=1.41—2.43 (m, 4H), 2.12 (s, 1H, NH), 2.83—3.42 (m, 2H, H-5), 4.08 (t, J=7.0 Hz, 1H, H-2), 7.03—7.60 (m, 5H).

2-Propylpiperidine (18): IR (neat) 1694, 1652, 1440, 1370, 1350, 1320, 1300, 1110, 1080, 1042, 868, 740 cm^{-1}; ^1H NMR (300 MHz) δ=0.89 (t, J=3.3 Hz, 3H, H-3′), 1.02—1.78 (m, 11H), 2.43 (br-d, J=10.5 Hz, 1H, H-2), 2.62 (dt, J=11.4, 2.7 Hz, 1H, H-6), 3.06 (br-d, J=11.7 Hz, 1H, H-6); ^{13}C NMR (76 MHz) δ=14.4, (C-3′), 19.2 (C-2′), 25.1 (C-1′), 26.8, 33.2, 39.9 (C-3), 47.4 (C-6), 56.7 (C-2); MS (20 eV) *m/z* (rel intensity) 127 (M^+, 3), 97 (6), 93 (6), 85 (7), 84 (100).

2-(2-Phenylethyl)piperidine (19): IR (neat) 1600, 1490, 1450, 1325, 1120, 1050, 740, 695 cm^{-1}; ^1H NMR (300 MHz) δ=1.08—1.80 (m, 9H), 2.45—2.67 (m, 4H), 3.04 (br-d, J=11.1 Hz, H-2), 7.12—7.48 (m, 5H); ^{13}C NMR (76 MHz) δ=25.0, 26.5, 32.3, 32.8, 39.4, 47.1 (C-6), 56.4 (C-2), 125.7, 128.4, 142.3; MS (20 eV) *m/z* (rel intensity) 190 (M^++1, 2), 189 (M^+, 4) 106 (6), 104 (6), 85 (6), 85 (100).

1,2,3,4-Tetrahydroisoquinoline (20): Bp 110—120 °C/6 mmHg (Kugelrohr). The spectral data were compared with those of commercially available sample.

(*R*)-(+)-*N*-Methyl-1-(4-chlorophenyl)ethylamine (22): ^1H NMR (270 MHz) δ=1.33 (d, J=6.6 Hz, 3H, CH_3), 2.20 (br, 1H, NH), 2.29 (s, 3H, NCH_3), 3.64 (q, J=6.6 Hz, 1H, CH), 7.21—7.32 (m, 4H, ArH). The optical purity was determined to be 98% ee as a corresponding *N*-benzoyl amide on the HPLC analysis using chiral column CHIRALCEL® OJ (eluent 2% ethanol in hexane, flow rate 1.0 mL min^{-1}).

Aqueous $TiCl_3$-Promoted Reduction of Hydroxamic Acid to Lactams. General Procedure: The preparation of 6-methoxy-3,4-Dihydro-2(1*H*)-quinolinone (**28**) is described as a typical example. To a solution of 6-methoxy-1-hydroxy-3,4-dihydro-2(1*H*)-quinolinone (**23**)

(0.430 g, 2.23 mmol) in THF (4.8 mL) was added an aqueous $TiCl_3$ (1.6 M, 3.0 mL, 4.8 mmol) at room temperature. After the mixture was stirred for 1 h, 5 M NaOH was added. The mixture was extracted with CH_2Cl_2, and the combined extracts were dried (Na_2SO_4) and evaporated to give **28** (0.389 g, 98%). Recrystallization from AcOEt gave analytical sample as a colorless prism (0.367 g, 93%): Mp 137.5—138.0 °C; ^{1}H NMR (270 MHz) δ=2.59 (d, J=8.8 Hz, 1H, H-3), 2.62 (d, J=8.0 Hz, 1H, H-3), 2.89 (d, J=8.0 Hz, 1H, H-4), 2.92 (d, J=8.8 Hz, 1H, H-4), 3.75 (s, 3H, OCH_3), 6.65—6.72 (m, 2H), 6.80—6.86 (m, 1H), 10.06 (br, 1H, NH); ^{13}C NMR (68 MHz) δ=25.4, 30.3, 55.3 (OCH_3), 112.1, 113.4, 116.3, 124.7, 130.8, 155.3, 172.1 (C=O).

Found: C, 67.87; H, 6.23; N, 7.95%. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.27; N, 7.90%.

3,4-Dihydro-(1*H*)-2-quinolinone (29): Mp 170.0—171.0 °C (recrystallized from AcOEt); IR (Nujol) 2955, 2854, 1462, 1377, 721 cm^{-1}; ^{1}H NMR (270 MHz) δ=2.63 (d, J=9.2 Hz, 1H, H-3), 2.66 (d, J=7.9 Hz, 1H, H-3), 2.96 (d, J=7.9 Hz, 1H, H-4), 2.98 (d, J=9.2 Hz, 1H, H-4), 6.85 (d, J=7.8 Hz, 1H), 6.98 (ddd, J=7.6, 7.6, 1.2 Hz, 1H), 7.12—7.21 (m, 2H), 9.22 (br, 1H, NH); ^{13}C NMR (68 MHz) δ=25.3, 30.7, 115.5, 123.0, 123.6, 127.5, 127.9, 137.3, 172.2 (C=O).

Found: C, 73.38; H, 6.19; N, 9.55%. Calcd for C_9H_9NO: C, 73.45; H, 6.16; N, 9.52%.

6-Methyl-3,4-dihydro-(1*H*)-2-quinolinone (30): Mp 136.0—136.5 °C (recrystallized from diisopropyl ether); IR (Nujol) 2955, 2926, 2845, 1682, 1464, 1377, 721 cm^{-1}; ^{1}H NMR (270 MHz) δ=2.29 (s, 3H, CH_3), 2.61 (d, J=9.4 Hz, H-3), 2.63 (d, J=7.9 Hz, 1H, H-3), 2.91 (d, J=7.9 Hz, 1H, H-4), 2.93 (d, J=9.4 Hz, H-4), 6.74 (d, J=8.4 Hz, 1H), 6.95—7.26 (m, 2H), 9.19 (br, 1H, NH); ^{13}C NMR (68 MHz) δ=20.7 (CH_3), 25.3, 30.8, 115.4, 123.5, 127.9, 128.5, 132.5, 134.8, 172.1 (C=O).

Found: C, 74.45; H, 6.90; N, 8.75%. Calcd for $C_{10}H_{11}NO$: C, 74.51; H, 6.88; N, 8.69%.

6-Bromo-3,4-dihydro-(1*H*)-2-quinolinone (31): Mp 177.5—178.5 °C (recrystallized from diisopropyl ether); ^{1}H NMR (270 MHz) δ=2.61 (d, J=9.2 Hz, 1H, H-3), 2.64 (d, J=8.0 Hz, 1H, H-3), 2.94 (d, J=8.0 Hz, 1H, H-4), 2.96 (d, J=9.2 Hz, H-4), 6.74 (d, J=8.9 Hz, 1H), 7.26—7.29 (m, 2H), 9.48 (br, 1H, NH); ^{13}C NMR (68 MHz) δ=25.0, 30.2, 115.3, 117.1, 125.5, 130.3, 130.6, 136.4, 172.3 (C=O).

Found: C, 48.06; H, 3.63; N, 6.24%. Calcd for C_9H_8NOBr: C, 47.82; H, 3.57; N, 6.20%.

6-Cyano-3,4-dihydro-(1*H*)-2-quinolinone (32): Mp 280 °C (decomp); ^{1}H NMR (270 MHz) δ=2.67 (d, J=9.2 Hz, H-3), 2.70 (d, J=8.0 Hz, 1H, H-3), 3.01 (d, J=8.0 Hz, 1H, H-4), 3.04 (d, J=9.2 Hz, H-4), 6.85 (d, J=8.6 Hz, 1H), 7.47—7.52 (m, 2H), 8.36 (br, 1H, NH); ^{13}C NMR (68 MHz) δ=25.0, 29.7, 106.3, 115.7, 118.7, 124.5, 131.8, 132.0, 141.1, 170.9 (C=O).

Stoichiometry of Aqueous $TiCl_3$ for Reduction of 1. An exactly weighed a 0.100 M solution of **1** was added dropwise to an aqueous $TiCl_3$ solution (1.61 M, 7.0 mL) at room temperature. After stirring for 15 min, the reaction mixture was diluted with water (20 mL). The resulting mixture was titrated with a standard $FeNH_4(SO_4)_2$ solution (0.2077 M) using a 10% KSCN (3 drops) as an indicator.[29] These results were listed in Table 4.

Stoichiometry of Anhydrous $TiCl_3$ for Dehydration of 1. To a stirred suspension of $TiCl_3$ in THF was added dropwise a solution of an exactly weighted **1** in THF at −78 °C. After the mixture was stirred for 15 min at room temperature, 1 M H_2SO_4 was added to the solution. The suspended solid was dissolved with stirring for 30 min. The resulting mixture was titrated with a standard $FeNH_4(SO_4)_2$ solution (0.2077 M) using a 10% KSCN (3 drops) as an indicator.[29] These results were listed in Table 5.

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